	12. (Amended) The isolated polynucle tide molecule of claim 11, wherein
	said nucleotide insertion, rearrangement, deletion or substitution specifies a phenotypic
3	alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size,
12°	or host range restriction[, or a change in an immunogenic epitope of PIV].
,	<u>or</u> need range restriction, or a change in an institute option of the
	15. (Amended) The isolated polynucleotide molecule of claim 11, wherein
	said polynucleotide sequence encoding said PIV genome or antigenome incorporates one or
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	more attenuating mutations of JS cp45.
	20. (Amended) The isolated polynucleotide molecule of claim 11, wherein
A 2	said polynucleotide sequence encoding said PIV genome or antigenome encodes an attenuating
65 1	
	amino acid substitution in the C protein.
	24 (Amended) The isolated aphymuologide molecule of claim 11 wherein
0.1	24. (Amended) The isolated polynucleotide molecule of claim 11, wherein
64	said polynucleotide sequence encoding said PIV genome or antigenome encodes an attenuating
`	amino acid substitution in the HN protein.
	26. (Amended) The isolated polynucleotide molecule of claim 11, wherein
1/2	said polynucleotide sequence encoding said PIV genome or antigenome incorporates at least
	one attenuating mutation in a 3' leader sequence.
	28. (Amended) The isolated polynucleotide molecule of claim 11, wherein
26	said polynucleotide sequence encoding said PIV genome or antigenome incorporates [a] an
10	attenuating mutation in a N gene start sequence.
	30. (Amended) The isolated polynucleotide molecule of claim 12, wherein
22	said polynucleotide sequence encoding said PIV genome or antigenome incorporates a
	plurality and up to a full complement of attenuating mutations present in rcp45, rcp45
	3'NCMFHN, rcp45 3'NL, rcp45 3'N, or rcp45 F.
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(Amended) The isolated polynucleotide molecule of claim 11, wherein 32. said polynucleotide sequence encoding said PIV genome or antigenome incorporates [a] an attenuating mutation stabilized by multiple nucleotide substitutions in a codon specifying the mutation. (Amended) The isolated polynucleotide molecule of claim 36, wherein 37. said one or more attenuating mutations of JS cp45 occur/in one or more PIV proteins selected from L, M, N, C, F, or HN or in a PIV extragenic sequence selected from a 3' leader or N-gene start sequence. (Amended) The isolated polynucleotide molecule of claim 33, wherein BID said chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations present in rcp45, rcp45 3'NCMFHN, rcp45 3'NL, rcp45 3'N, or rcp45 F. (Amended) The method of claim 52, wherein the polynucleotide 65. molecule encoding the PIV genome or antigenome incorporates at least one attenuating mutation of JS cp45. 12 67. (Amended) The method of claim 65, wherein the mutation of JS cp45 specifies at least one attenuating amino acid substitution in the polymerase L protein. 69. (Amended) The method of claim 65, wherein said mutation of JS cp45 specifies [a] an attenuating change in a PIV protein selected from L, M, N, C, F, or HN or in a PIV extragenic sequence selected from a 3' leader or N gene start sequence. 70. (Amended) /The method of claim 52, wherein said polynucleotide molecule encoding the PIV genome or antigenome incorporates [a] an attenuating mutation that is stabilized by multiple nucleotide substitutions in a codon which specifies the mutation. 71. (Amended) The method of claim 52, wherein said polynucleotide

molecule encoding said PIV/genome or antigenome incorporates a plurality and up to a full

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-complement of <u>attenuating</u> mutations present in rcp45, rcp45 3'NCMFHN, rcp45 3'NL, rcp45 3'N, or rcp45 F.

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78. (Amended) The method of claim 73, wherein said chimeric genome or lantigenome incorporates one or more attenuating mutations of JS cp45.

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80. (Amended) The method of claim/73, wherein a mutation specifying a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV] is incorporated in a chimeric PIV background comprising a genome or antigenome having one or more PIV3 HN or F glycoprotein genes substituted by one or more counterpart PIV1 or PIV2 HN and F glycoprotein genes.

- 88. (Amended) The method of claim 52, wherein the polynucleotide molecule encoding the PIV genome or antigenome is selected from:
  - i) p218(131) (SEQ ID NO: 1);
  - ii) p3/7(131) (SEQ ID NO: 14);
  - iii) p3/7(131)2G (SEQ/ID NO: 15); or
- iv) the polynucleotide molecule of i), ii) or iii) modified by introduction of a heterologous PIV sequence selected from a HPIV1 sequence, a HPIV2 sequence, a BPIV sequence or a MPIV sequence or by a nucleotide insertion, rearrangement, deletion or substitution specifying a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV].

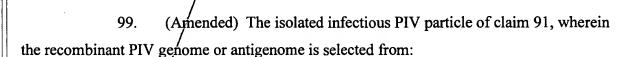
/

- 89. (Amended) The method of claim 52, wherein the polynucleotide molecule encoding the PIV genome or antigenome is selected from:
  - i) p218(131) (SEQ ID NO: 1);
  - ii) p3/7(131) (SEQ ID NO: 14);
  - iii)  $p_3^3/7(131)2G$  (SEQ ID NO: 15); or

iv) the polynucleotide molecule of i), ii) or iii) modified by introduction of a heterologous PIV sequence selected from a HPIV1 sequence, a HPIV2 sequence, a BPIV sequence or a MPIV sequence and by a nucleotide insertion, rearrangement, deletion or substitution different from said introduction of said heterologous PIV sequence specifying a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV].

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- 90. (Amended) The method of claim 52, wherein the <u>infections PIV particle</u> is attenuated and wherein the polynucleotide molecule encoding the PIV genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting a protective immune response in a mammalian host.
- 98. (Amended) The isolated infectious PIV particle of claim 91, wherein the recombinant PIV genome or antigenome is selected from:
  - i) p218(131) (SEQ ID/NO: 1);
  - ii) p3/7(131) (SEQ ID NO: 14);
  - iii) p3/7(131)2G (SÉQ ID NO: 15); or
- iv) the genome or antigenome of i), ii) or iii) modified by introduction of a heterologous PIV sequence selected from a HPIV1 sequence, a HPIV2 sequence, a BPIV sequence or a MPIV sequence or by a nucleotide insertion, rearrangement, deletion or substitution specifying a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV].



- i) /p218(131) (SEQ ID NO: 1);
- ii) p3/7(131) (SEQ ID NO: 14);
- iii) / p3/7(131)2G (SEQ ID NO: 15); or



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- iv) the genome or antigenome of i), ii) or/iii) modified by introduction of a heterologous PIV sequence selected from a HPIV1 sequence, a HPIV2 sequence, a BPIV sequence or a MPIV sequence and by a nucleotide insertion, rearrangement, deletion or substitution different from said introduction of said heterologous PIV sequence specifying a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV].
- 102. (Amended) The isolated infectious PIV particle of claim 91, wherein the recombinant PIV genome or antigenome is modified by a nucleotide insertion, rearrangement, deletion or substitution encoding a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV].

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105. (Amended) The isolated infectious PIV particle of claim 91, wherein the recombinant PIV genome or antigenome incorporates at least one attenuating mutation of JS cp45.

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109. (Amended) The isolated infectious PIV particle of claim 97, wherein said chimeric genome or antigenome incorporates one or more attenuating mutations of JS cp45.

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111. (Amended) The isolated infectious PIV particle of claim 109, wherein said chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations present in rcp45, rcp45 3'NCMFHN, rcp45 3'NL, rcp45 3'N, or rcp45 F.

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112. (Amended) The isolated infectious PIV particle of claim 91, wherein a mutation specifying a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV] is incorporated in a chimeric PIV background comprising a genome or antigenome having one or more PIV3 HN or F glycoprotein genes or gene segments

substituted by one or more counterpart PIV1 or PIV2 HN and F glycoprotein genes or gene segments. (Amended) The isolated infectious PIV particle of claim 112, wherein 113. one or more attenuating mutations of JS cp45 are incorporated in said chimeric background. (Amended) The isolated infectious PIV particle of claim 91 which is 115. attenuated, wherein the recombinant PIV genome of antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting a protective immune response in a mammalian host. (Amended) The isolated infectious PIV particle of claim 91, which is attenuated and is selected from r942, r992, r/1558, r942/992, r992/1558, r942/1558, or r942/992/1558, rep45 3'N, rep45 C, rep45 M, rep45 F, rep45 HN, rep45L, rep45 3'NL, rep45 3'NCMFHN, and rcp45. 125. (Amended) The immunogenic composition of claim 123, wherein the recombinant PIV genome or antigenome of said infectious, chimeric PIV particle is modified by a nucleotide insertion, rearrangement, deletion or substitution encoding a phenotypic alteration selected from attenuation, temperature-sensitivity, cold-adaptation, small plaque size, or host range restriction[, or a change in an immunogenic epitope of PIV]. 127. (Amended) The immunogenic composition of claim 118, wherein the recombinant PIV genome or antigenome incorporates [a] an attenuating mutation of JS cp45. (Amended) The isolated polynucleotide molecule of claim 129, wherein 130. the isolated polynucleotide encoding the chimeric PIV genome or antigenome further

incorporates one or more attenuating mutations of JS cp45.

827 2000) the isolated polynucleotide encoding the chimeric PIV genome or antigenome further incorporates a full complement of attenuating mutations present in JS cp45, said full complement of mutations comprising i) substitutions specifying a replacement of His for Tyr942, Phe for Leu992, and Ile for Thr 1558 in the polymerase L protein; ii) substitutions specifying a replacement of Ala for Val96 and Ala for Ser389 in the N protein; iii) a substitution specifying a replacement of Thre for Ile96 in the C protein[; iv) substitution specifying an amino acid change in the F protein comprising a replacement of Val for Ile420 or Thr for Ala450; v) substitutions specifying a replacement of Ala for Val384 in the HN protein; vi) a-substitution specifying a replacement of Thr for Pro199 in the M protein; vii) [v) mutations in a 3' leader sequence comprising a T to C change at a position corresponding to nucleotide 23 of JS cp45, a C to T change at nucleotide 24, a G to T change at nucleotide 28, and a T to A change at nucleotide 45 of JS cp45; and [viii)[vi] a mutation in an N gene start sequence comprising an A to T change at a position corresponding to nucleotide 62 of JS cp45.

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said chimeric genome or antigenome incorporates a full complement of attenuating mutations present in JS cp45, said full complement of attenuating mutations comprising i) substitutions specifying a replacement of His for Tyr942, Phe for Leu992, and Ile for Thr1558 in the polymerase L protein; ii) substitutions specifying a replacement of Ala for Val96 and Ala for Ser389 in the N protein; iii) a substitution specifying a replacement of Thre for Ile96 in the C protein[; iv) substitution specifying-an-amino acid change-in-the-F-protein comprising a replacement of Val for Ile420 or Thr for Ala450; v) substitutions specifying a replacement of Ala for Val384-in-the HN protein; vi) a substitution specifying a replacement of Thr for Pro199 in-the M-protein; viii)] (v)/mutations in a 3' leader sequence comprising a T to C change at a position corresponding to nucleotide 23 of JS cp45, a C to T change at nucleotide 24, a G to T change at nucleotide 28, and a T to A change at nucleotide 45 of JS cp45; and [viii)] vi) a mutation in an N gene start sequence comprising an A to T change at a position corresponding to nucleotide 62 of JS cp45.

out ) ent/ B 29 antigenome incorporates a full complement of mutations present in JS cp45, said full complement of attenuating mutations comprising i) substitutions specifying a replacement of His for Tyr942, Phe for Leu992, and the for Thr1558 in the polymerase L protein; ii) substitutions specifying a replacement of Ala for Val96 and Ala for Ser389 in the N protein; iii) a substitution specifying a replacement of Thre for Ile96 in the C protein[; iv) substitution specifying an amino acid change in the F protein comprising a replacement of Val for Ile420 or Thr for Ala450; v) substitutions specifying a replacement of Ala for Val384 in the HN protein; vi) a substitution specifying a replacement of Thr for Pro199 in the M protein; vii)] (v) mutations in a 3' leader sequence comprising a T to C change at a position corresponding to nucleotide 23 of JS cp45, a C to T change at nucleotide 24, a G to T change at nucleotide 28, and a T to A change at nucleotide 45 of JS cp45; and [viii)] vi) a mutation in an N gene start sequence comprising an A to T change at a position corresponding to nucleotide 62 of JS cp45.

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138. (Amended) The isolated infectious PIV particle of claim 137, wherein the recombinant PIV genome or antigenome further incorporates one or more attenuating mutations of JS cp45.

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140. (Amended) The isolated infectious PIV particle of claim 137, wherein the isolated polynucleotide encoding the chimeric PIV genome or antigenome further incorporates a full complement of attenuating mutations present in JS cp45, said full complement of mutations comprising i) substitutions specifying a replacement of His for Tyr942, Phe for Leu992, and Ile for Thr1558 in the polymerase L protein; ii) substitutions specifying a replacement of Ala for Val96 and Ala for Ser389 in the N protein; iii) a substitution specifying a replacement of Thre for Ile96 in the C protein; iv) substitution specifying an amino acid change in the F protein comprising a replacement of Val for Ile420 or Thr for Ala450; v) substitutions specifying a replacement of Ala for Val384 in the HN protein; vi) a substitution specifying a replacement of Thr for Pro199 in the M protein; vii)] (v) mutations in a 3' leader sequence comprising a T to C change at a position corresponding to nucleotide 23 of JS cp45, a C to T change at nucleotide 24, a/G to T change at nucleotide 28, and a T to A change at

nucleotide 45 of JS cp45; and [viii)] vi) a mutation in an N gene start sequence comprising an A to T change at a position corresponding to nucleotide 62 of JS cp45.

141. The isolated infectious PIV particle of claim 111, wherein said chimeric PIV genome or antigenome further incorporates the full complement of mutations present in JS cp45, said full complement of mutations comprising i) substitutions specifying a replacement of His for Tyr942, Phe for Leu992, and the for Thr1558 in the polymerase L protein; ii) substitutions specifying a replacement of Ala for Val96 and Ala for Ser389 in the N protein; iii) a substitution specifying a replacement of Thre for Ile96 in the C protein[; iv) substitution specifying an amino acid change in the F protein comprising a replacement of Val for Ile420 or Thr for Ala450; v) substitutions specifying a replacement of Ala for Val384 in the HN protein; vi) a substitution specifying a replacement of Thr for Pro199 in the M protein; vii)] (v) mutations in a 3' leader sequence comprising a T to C change at a position corresponding to nucleotide 23 of JS cp45, a C to T change at nucleotide 24, a G to T change at nucleotide 28, and a T to A change at nucleotide 45 of JS cp45; and [viii)] vi) a mutation in an N gene start sequence comprising an A to T change at a position corresponding to nucleotide 62 of JS cp45.

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143. (Amended) The immunogenic composition of claim 142, wherein said recombinant PIV genome or antigenome further incorporates a full complement of attenuating mutations present in JS cp45, said full complement of mutations comprising i) substitutions specifying a replacement of His for Tyr942, the for Leu992, and Ile for Thr1558 in the polymerase L protein; ii) substitutions specifying a replacement of Ala for Val96 and Ala for Ser389 in the N protein; iii) a substitution specifying a replacement of Thre for Ile96 in the C protein[; iv) substitution specifying an amino acid change in the F protein comprising a replacement of Val for Ile420 or Thr for Ala450; v) substitutions specifying a replacement of Ala for Val384 in the HN protein; vi) a substitution specifying a replacement of Thr for Pro199 in the M protein; vii)] (v) mutations in a 3' leader sequence comprising a T to C change at a position corresponding to nucleotide 23 of JS cp45, a C to T change at nucleotide 24, a G to T change at nucleotide 28, and a T to A change at nucleotide 45 of JS cp45; and [viii)] vi) a mutation in an N gene start sequence comprising an A to T change at a position corresponding to nucleotide 62 of JS cp45.

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